Prognostic Factors and Surgical Approach

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ESO-ESMO Berlin Masterclass 2018
Disclosures

Remuneration for scientific presentations and participation on Advisory Boards: *Merck Serono, Roche, Astra Zeneca, MSD, BMS*

Research Support: *Roche, Merck Serono*
Prognoses and improvement for head and neck cancers diagnosed in Europe (EUROCARE-5)

Gatta E. et al.: EUROCare-5, HNSCC diagnosed early 2000s; EJC 2015
Age-standardised 5-year relative survival (%) 2000–2007

Mundhöhle | Oropharynx | Nasopharynx | Hypopharynx | Larynx
---|---|---|---|---

Gatta E. et al.: EUROCARE-5, HNSCC diagnosed early 2000s; EJC 2015
Predictive factors

• TNM
• Tumor volume
• Degree of resection margin (R0 versus R+)
• HPV 16, p16
266 Patients with oropharyngeal cancer, known tumor HPV status, and known number of pack-years of smoking

178 Had HPV-positive tumors
- 88 Had ≤10 pack-years
  - 26 Had N0–N2a cancer
  - 64 Had N2b–N3 cancer
- 90 Had >10 pack-years
  - 15 Had T2–T3 tumors
- 23 Had ≤10 pack-years
- 88 Had HPV-negative tumors
- 65 Had >10 pack-years

114 of 266 (42.9%) were at low risk
79 of 266 (29.7%) were at intermediate risk
73 of 266 (27.4%) were at high risk

K. Kian Ang et al.
A

![Graph A](image1.png)

**Survival (probability)**

- I (n = 8)
- II (n = 25)
- III (n = 79)
- IV (n = 461)

**Time (years)**

P = .58

**HPV-related**

B

![Graph B](image2.png)

**Survival (probability)**

- I (n = 8)
- II (n = 31)
- III (n = 38)
- IV (n = 160)

**Time (years)**

P = .004

**HPV-non-related**
Current opinion on resection margins

R0 ideal = 5mm

R1, 2 high risk
R0 <5mm intermediate risk
R0 >5mm low risk
principles in therapy

Squamous cell carcinoma head and neck

Resectable
- Organ preserving surgery
- Ablative surgery

Non-resectable
- Organ preserving chemotherapy
- Chemo-radiation

Adjuvant radio-, radiochemo-therapy

Salvage surgery

Palliative chemotherapy

First line
Second line

17th ESO-ESMO Masterclass Clinical Oncology
Transoral vs. open resection
"ERAS" of TRANSORAL APPROACHES

1971: Laser coupled to microscope
1989: 1st TLM OP paper
2005: "Inside out" OP operations perfected
2008: 5 continents Congress, Göttingen
2009: Bleeding mx, CTA-3D recon (Salassa)
2011: HPV reporting

Larger #s reported
Multicenter study

TLM

Courtesy of Bruce Haughey

17th ESO-ESMO Masterclass Clinical Oncology
• Cave: even after ligation of ACE sever beeding possible!
Robotic-Assisted Surgery
Balancing Evidence and Implementation

Jason D. Wright, MD

“Without clear demonstration of improved outcomes associated with robotic-assisted procedures, the complicated issue of the cost will become increasingly important”.

“Both the generation of high quality evidence evaluating new procedures and then the utilization of this evidence to guide practice should remain priorities for surgical disciplines”.
Flex-Robotic System Head and Neck
Smaller, smarter, cheaper
Überleben nach primärer laser resection (TLM)
204 Oropharynx-Karzinompatienten, p16 positiv

ECS ist kein prognostischer Faktor bei p16-positiven Oropharynxkarzinomen


$P = 0.68$
Advanced OPSCC

T3/4 OPSCC: transoral/open transpharyngeal resection, reconstruction with free forearm flap, bilat. Selective Neck dissection + adj. PORCT
Advanced OPSCC
Reconstruction with free forearm flab
Functional outcome in patients with advanced head and neck cancer: surgery and reconstruction with free faps versus primary radiochemotherapy: **ICF Core Sets for HNC**

<table>
<thead>
<tr>
<th>ICF category</th>
<th>Title</th>
<th>ProbChiSq</th>
<th>ORE</th>
<th>LowerCL</th>
<th>UpperCL</th>
<th>More problems in group</th>
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<tbody>
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<td><strong>Body structures (n = 3)</strong></td>
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<tr>
<td>s420</td>
<td>Structures of immune system, e.g. lymph nodes</td>
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<td>0.03</td>
<td>0.52</td>
<td>MVFF</td>
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<td>b51050</td>
<td>Oral swallowing</td>
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<td>1.06</td>
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<td>RCT</td>
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<td>b530</td>
<td>Weight maintenance functions</td>
<td>0.00</td>
<td>10.24</td>
<td>3.02</td>
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<td>1.12</td>
<td>19.91</td>
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<td><strong>Activities &amp; participation (n = 6)</strong></td>
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<td>d240</td>
<td>Handling stress and other psychological demands</td>
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<td>3.13</td>
<td>1.08</td>
<td>9.04</td>
<td>RCT</td>
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<tr>
<td>d360</td>
<td>Using communication devices and techniques</td>
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<td>1.28</td>
<td>23.4</td>
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<tr>
<td>d750</td>
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<td>1.27</td>
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<td>d845</td>
<td>Acquiring, keeping and terminating a job</td>
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<td>d870</td>
<td>Economic self-sufficiency</td>
<td>0.01</td>
<td>5.69</td>
<td>1.63</td>
<td>19.83</td>
<td>RCT</td>
</tr>
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</table>

*Probabilities (P) are calculated using the Chi-square test.*

**Table 1:** Comparison of mean (SD) values for MVFF and pRCT, with P values and significance levels.

- Overall health, patient perspective EORTC-c30, quest. no. 29: MVFF 5.13 (1.2), pRCT 4.09 (1.5), P = 0.015 (n.s., *no difference*).
- Overall QOL, patient perspective EORTC-c30, quest. no. 30: MVFF 4.70 (1.6), pRCT 4.48 (1.3), P = 0.590 (n.s., *no difference*).
- Health-related QOL, patient perspective UW-QOL, quest. no. 14: MVFF 2.52 (1.3), pRCT 3.75 (1.4), P = 0.051 (n.s., *no difference*).
- Health-related QOL, patient perspective UW-QOL, quest. no. 15: MVFF 3.36 (1.0), pRCT 4.25 (0.8), P = 0.036 (n.s., *no difference*).
- Overall QOL, patient perspective UW-QOL, quest. no. 16: MVFF 3.41 (1.1), pRCT 3.75 (0.8), P = 0.403 (n.s., *no difference*).
- ICF Summary score: MVFF 59.3 (19.5), pRCT 79.9 (43.3), P = 0.032 (n.s., *no difference*).

**Note:**
- n.s. not significant (P > 0.05)
- * Significant with P < 0.05

**Reference:**
Tschiesner U. et al: Eur Arch Otorhinolaryngol 2011
Treatment Deintensification in Human Papillomavirus-Positive Oropharynx Cancer: Outcomes From the National Cancer Data Base

Cheraghlou et al. 2017

- retrospektive; all HPV16+ patients

Stage I (T1-2 N0-1) n=3198

AJCC 8. Edition
The Role of Adjuvant Chemotherapy in Surgically Managed, p16-Positive Oropharyngeal Squamous Cell Carcinoma

Skillington et al JAMA Otolaryngol Head and Neck Surg 2017 Mar 1;143(3):253-259

- OPC HPV-16+
- Kohort study 1996 – 2010, non prospektive study
- High-risk
- CRT = 90 patients und RT = 88 patients

5- Y OS
CRT  82%
RT     84%
Stage II (T1-2 N2, T3N0-2)
n = 795    AJCC 8. Edition

„CONCLUSION: Deintensification of treatment from chemoradiotherapy to radiotherapy or surgery alone in cases of HPV16 (AJCC 8. edition) stage I or stage II disease may compromise patient safety.”
Treatment Outcomes for T4 Oropharyngeal Squamous Cell Carcinoma


- retrospektive cohort analysis T4a,b- OPC Patienten
- HPV positive + HPV negative
- HPV 16 + -non-surgery (ICT+RT,CRT) 47 patients
- HPV16 + - surgery 50 patients
Stage III (T1-4 N3, T4 N0-3)  
n = 450

„CONCLUSION: Treatment intensification to triple-modality therapy for patients with stage III disease may improve survival in this group”
WP, männlich, 59 Jahre

Staging:

• Panendoskopie: < 2 cm linker Zungengrundtumor
• NMR: 16 mm größte Ausdehnung; links Level II (33 mm)
• FDG PET-CT: M0
• Grade 1 HNSCC, p16+/HPV+
WP, männlich, 59 Jahre

In 2014...

- **UICC/AJCC 7th ed:** T1-N2a-M0 + ECS (stage IV)

**Treatment:**

- primary transoral surgery + adjuvant Concomitant chemo-radiotherapy (60 Gy in 6w + 2 courses of 100 mg/m2 cddp)

- Alternatively: Primary treatment: Concomitant chemo-radiotherapy (70 Gy in 6w + 2 courses of 100 mg/m2 cddp)
WP, männlich, 59 Jahre

In 2018...

• **UICC/AJCC 8th ed: T1-N1-M0 (stage I)**

Treatment:

• primary transoral surgery + adjuvant Concomitant chemo-radiotherapy (60 Gy in 6w + 2 courses of 100 mg/m² cddp)

• Alternatively: Primary treatment: Concomitant chemo-radiotherapy (70 Gy in 6w + 2 courses of 100 mg/m² cddp)

**Cave: Downstaging**
principles in therapy

- Squamous cell carcinoma head and neck

  - Resectable
  - Organ preserving surgery
  - Adjuvant radio-, radiochemo-therapy
  - Ablative surgery
  - Adjuvant radio-, radiochemo-therapy
  - Organ preserving chemoradiation
  - Salvage surgery

  - Non resectable
  - Chemo-radiation
  - Salvage surgery

  - Palliative chemotherapy
    - First line
    - Second line
T4a-Larynx carcinoma
Voice Prothesis: example PROVOX I/II
Late toxicity

“laryngo-esophageal dysfunction-free survival” after 5 years

Ratio of patients with larynx oedema grade 3 or 4

Dose to the larynx (Gy)
Overall survival Laryngektomy vs. multimodal organ preservation T4a-Larynx carcinoma (969 Patients, 64% LP, 36% TL, retrospektive NCDB)

Kaplan-Meier Kurven: Overall survival Laryngetomie vs. multimodaler Organerhalt T4a-Larynxkarzinome (Grover S et al.)
Laryngektomie (TL) und post operative radiotherapie (PORT) ist superior compared with multimodale organ preservation therapy adressing late functional outcome

Kaplan-Meier Kurven: “laryngoesophageal dysfunction-free survival” (LEDFS), “laryngectomy-free survival” (LxFS), “actuarial freedom from laryngoesophageal dysfunction” (FFLED), und “actuarial freedom from laryngectomy” (FFL) innerhalb der Gruppe von multimodal, also nicht chirurgisch behandelten Patienten (60 Patienten). (Rosenthal DI et al)
Two-thirds of patients \((n = 38)\) were not suitable for salvage surgery because of

- distant metastases \((n = 30)\)
- poor general condition of the patient \((n = 3)\)
- refusal of surgery by the patient \((n = 1)\)
- unresectability of the tumour \((n = 4)\)
Salvage surgery in post-chemoradiation laryngeal and hypopharyngeal carcinoma: outcome and review

Chirurgia di salvataggio nel carcinoma della laringe o dell’ipofaringe post-chemioradioterapia: risultati e revisione della letteratura

L. VAN DER PUTTEN1,2, R. DE BREE3, P.A. DOORNAERT4, J. BUTER5, S.E.J. EERENSTEIN1, D.H.F. RIETVELD4, D.J. KUIK6, C.R. LEEMANS1

Acta Otorhinolaryngol Ital 2015;35:162-172

<table>
<thead>
<tr>
<th>Complications</th>
<th>Total</th>
<th>Pharynx open</th>
<th>Pharynx closed</th>
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<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>None</td>
<td>7</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Wound healing</td>
<td>13</td>
<td>9</td>
<td>4</td>
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<tr>
<td>- Infection or dehiscence</td>
<td>7</td>
<td>5</td>
<td>2</td>
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<tr>
<td>- Haemorrhage</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>- Fistula</td>
<td>5</td>
<td>4</td>
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<tr>
<td>Pneumonia</td>
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<tr>
<td>Other</td>
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</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>15</td>
<td>7</td>
</tr>
</tbody>
</table>

Complete response
Recurrence with salvage
Recurrence without salvage

Probability
Months
Trends in treatment and survival for advanced laryngeal cancer: A 20-year population-based study in The Netherlands

Adriana J. Timmermans, MD, Boukje A. C. van Dijk, PhD, Lucy J. H. Overbeek, PhD, Marie-Louise F. van Volthuysen, MD, PhD, Harm van Tinteren, PhD, Frans J. M. Hilgers, MD, PhD, Michel W. M. van den Brekel, MD, PhD.

Department of Head and Neck Oncology and Surgery, The Netherlands Cancer Institute, Amsterdam, The Netherlands, Netherlands Comprehensive Cancer Organisation, Department of Research, Utrecht, The Netherlands, University of Groningen, University Medical Centre Groningen, Department of Epidemiology, Groningen, The Netherlands, PALGA (the Dutch nationwide network and registry of histopathology and cytopathology), Leiden, The Netherlands, Department of Pathology, the Netherlands Cancer Institute, Amsterdam, The Netherlands, Biostatistics Department, the Netherlands Cancer Institute, Amsterdam, The Netherlands, Institute of Phonetic Sciences, University of Amsterdam, Amsterdam, The Netherlands, Department of Oral and Maxillofacial Surgery, Academic Medical Center, Amsterdam, The Netherlands.


5-year overall survival:
Total laryngectomy: 49%
Radiotherapy: 47%
Radio- and chemotherapy: 43%

p=0.539

Cum Survival

Primary treatment

Total laryngectomy
Radiotherapy
Radio- and chemotherapy

T3

TL
142
121
94
84
65
52

T4

TL
123
96
71
64
53
44

5-year overall survival:
Total laryngectomy: 48%
Radiotherapy: 34%
Radio- and chemotherapy: 42%

p<0.0001

Cum Survival

Primary treatment

Total laryngectomy
Radiotherapy
Radio- and chemotherapy

Michiel van den Brekel
Neck dissection: Classification of Robbins
rare indication today
Neck Dissection

- **radical Neck Dissektion (RND)**
  Resection Level I-V incl. Resection of VJI, M.SCCM and N.accessorius

- **modified radical Neck Dissektion (mRND) = functional ND**
  Resection of Level I-V; preservation of 1 or more non-lymphatic structures of RND

- **selektive Neck Dissektion (SND)**
  Preservation of 1 or more LK-levels of RND; preservation of VJI, M.SCM and N.accessorius
  **new**: SND I-III   **old**: supraomohyoidal SND

- **extended Neck Dissektion**
The Effect of Treating Institution on Outcomes in Head and Neck Cancer

Amy Anne D. Lassig, MD\textsuperscript{1}, Anne M. Joseph, MD, MPH\textsuperscript{2}, Bruce R. Lindgren, MS\textsuperscript{3}, Patricia Fernandes, DDS\textsuperscript{1}, Sarah Cooper\textsuperscript{1}, Chelsea Schotzko\textsuperscript{1}, Samir Khariwala, MD\textsuperscript{1}, Margaret Reynolds, MD\textsuperscript{4}, and Bevan Yueh, MD, MPH\textsuperscript{1}

Categorical Data Items

<table>
<thead>
<tr>
<th>Type of radiation</th>
<th>Community, No. (%)</th>
<th>Academic, No. (%)</th>
<th>(P) Value$^a$</th>
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<tr>
<td>Primary</td>
<td>64 (44.1)</td>
<td>100 (47.6)</td>
<td>.447</td>
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<td>Adjuvant</td>
<td>79 (54.5)</td>
<td>104 (49.5)</td>
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<td>2 (1.4)</td>
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<td>Primary or adjuvant without chemotherapy</td>
<td>69 (47.6)</td>
<td>60 (28.6)</td>
<td>(&lt;.001^b)</td>
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<td>Primary or adjuvant with chemotherapy</td>
<td>74 (51.0)</td>
<td>144 (68.6)</td>
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<tr>
<td>Unknown</td>
<td>2 (1.4)</td>
<td>6 (2.9)</td>
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</table>

\(P\) values are for the comparison between community and academic institutions.
Summary

- Primary surgery is only recommended if R0 resection is possible and reasonable functional outcome available.
- Reconstruction is highly developed and free flap techniques offer a broad spectrum of possibilities.
- Transoral technologies like TORS and TLM are coming more in focus for oropharyngeal and laryngeal/hypopharyngeal HNSCC.
- TORS stimulates a fruitful debate about less mutilating surgery.
- HPV-positivity has no impact on standard treatment (first results of deescalation trials are expected 2021)
- Neck dissection has to be performed by separating the neck levels for better classification of the pathologist.
- Currently the EORTC H&N Group is working on a QA Surgery to standardize quality criteria for H&N institutions regarding future clinical trials.
UPDATE SKILLS IN HEAD AND NECK SURGERY AND ONCOLOGY

27-29 September 2018 - Leipzig, Germany

Course Director: A. Dietz, DE
Organising Committee: S. Wiegand, DE - G. Willemsen, DE - C. Standke, DE - R. Wyrras, DE - J. Leupold, DE

KLINIK UND POLIKLINIK FÜR HALS-, NASEN- UND OHRENHEILKUNDE